REMARKS / ARGUMENTS

Claims 1, 2 and 4-7 are pending in this application. Claims 1 and 6 are amended.

The amendment to claim 1 is supported by the specification at page 3, fourth paragraph.

Applicants submit that the amendment to claim 6 overcomes the rejection of it under 35 USC 112, second paragraph. The claim no longer refers to "Compound I" and reference to calculating the dose of a pharmaceutical based on the amount of free base is common in the art. Thus, Applicants assert that present claim 6 is definite and withdrawal of this rejection is requested.

Claims 1, 2 and 4-7 were rejected under 35 USC 103(a) over Zimmermann et al in light of Mouriaux et al in view of Ijland et al.

At page 12 of the Office action dated July 24, 2007, which is cited in the present Office action, the Examiner relies on Mouriaux et al to support, as fact, the alleged teaching that activation of c-kit by its ligand contributes to the proliferation of choroidal melanocytes. The Examiner concludes that Mouriaux et al provides a reasonable expectation that uveal melanoma cells would have expressed c-kit because the reference allegedly teaches the correlation of c-kit activation and proliferation of melanocytes in the eye that contribute to formation of uveal tumors. However, the reference is clear that the addition of SCF (c-kit ligand) to the medium did not change melanocyte morphologies and did not induce proliferation in the absence of two other factors. See paragraph bridging pages 153 and 154 and following paragraphs. Indeed, the article concludes that the experiments demonstrate that SCF was mitogenic only in the presence of other factors. Applicants assert that such a disclosure does not lead the skilled artisan to reasonably expect that a c-kit inhibitor, such as imatinib, would be useful for treating uveal melanoma. At best, it suggests that further experiments should be conducted. Thus, reliance on Mouriaux et al in the present rejection is improper.

Ijland et al is relied upon as disclosing that uveal melanoma cell lines express VEGF, an important angiogenesis growth factor. Zimmermann et al is relied upon as disclosing that imatinib inhibits the angiogenesis effect of VEGF. The Examiner concludes that these disclosures provide the skilled artisan with a reasonable expectation that imatinib would successfully treat uveal melanoma.

Applicants assert that these disclosures reasonably provide no more than a basis to hypothesize that imatinib may be useful for the treatment of uveal melanoma. However, in an

unpredictable art like the treatment of cancer, where many such experiments fail, the skilled artisan would not have a reasonable expectation of success until experiments designed to test the hypothesis were carried out and successful. Such experiments are not reported in the cited art. Thus, Applicants assert that the rejection is based on hindsight and that the experiments which provide the skilled artisan with a reasonable expectation of success are not found in the cited art, but instead, and impermissibly so, based on the experiments disclosed in the present specification. Therefore, the presently claimed invention is not *prima facie* unpatentable under 35 USC 103(a).

Although Applicants assert that the claimed invention is not *prima facie* obvious over the cited art for the reasons discussed above, and, for that reason, no data demonstrating unexpected results is needed to establish the patentability of the present invention, the present specification contains data demonstrating the extraordinary efficacy of imatinib mesylate against several uveal melanoma cell lines.

In the recent Office action, the Examiner indicates that the data does not support the patentability of the claimed invention for reasons that are addressed below.

Claim 1 is now amended to require administration of a therapeutically effective dose of imatinib.

The skilled artisan would readily understand that the experiments reported in Example 1 were done twice and that the result for each is reported.

The first paragraph on page 2 of the specification indicates that the free base, imatinib, corresponds to the active moiety. Thus, the skilled artisan would reasonably expect the pharmaceutically acceptable counter ion in a quaternary ammonium salt of the free base to have little effect on the therapeutic properties of the compound and expect that similar results would be found with other salts. Therefore, it is reasonable to rely on data from the mesylate salt for the patentability of the full range of pharmaceutically acceptable salts.

The Ljland et al reference indicates that uveal melanoma has a high mortality rate with a short survival time once hepatic metastases are diagnosed. Clearly, there is a need for a therapy to improve such a dire prognosis.

The Office action goes into great detail about the perceived shortcomings of the data presented in Example 1. The Examiner appears to agree that the data shows an unexpected effect with respect to certain cell lines at certain concentrations and incubation times. However,

the Examiner points out that the claims are not limited to those cell lines, concentrations and incubation times.

Applicants' invention is not limited to specific cell lines, concentrations and incubation times. There is a clear effect in all cell lines at the high doses after 48 hours. Indeed, in each of the cell lines at least 75% of the cells die after 48 hours at the 5 and 10 μM concentrations and a clear dose response over all concentrations is seen in 2 cell lines. Thus, Applicants' invention is the use of imatinib for the treatment of uveal melanoma, which is what the claims cover. Applicants assert that the cited art does not predict such effects and that such effects support the patentability of the claimed invention over the full range of the present claims; especially in view of the extensive clinical experience with imatinib since its approval in 2001 as a targeted cancer therapy.

Applicants request withdrawal of the rejection under 35 USC 103(a) in view of the discussion above.

Entry of this amendment and reconsideration and allowance of the claims is respectfully requested.

Respectfully submitted,

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